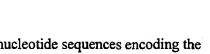
WE CLAIM:

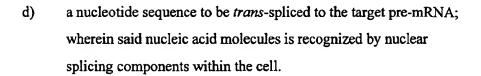
- 1. A nucleic acid molecule comprising:
 - a) two or more target binding domains that target binding of the pretrans-splicing molecule to a target pre-mRNA;
 - b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site and a 5' splice donor site;
 - c) spacer regions that separate the 3' splice region and the 5' splice donor site from the target binding domains; and
 - d) a nucleotide sequence to be trans-spliced to the target pre-mRNA; wherein said nucleic acid molecules is recognized by nuclear splicing components within the cell.
- 2. The nucleic acid molecule of claim 1 wherein the spacer regions separate the 3' splice region and the 5' splice donor site from the target binding domains.
- 3. The nucleic acid molecule of claim 1 wherein the nucleic acid molecule further comprises sequences encoding a translatable protein product.

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- 4. The nucleic acid molecule of claim 3 wherein the translatable protein product is a toxin.
- 5. The nucleic acid molecule of claim 1 wherein the nucleic acid molecule further comprises sequences containing a translational stop codon.
- 6. The molecule of claim 1 wherein the nucleotide sequence to be *trans*-spliced to the target pre-mRNA comprises nucleotide sequences encoding the cystic fibrosis trans-membrane conductance regulator.



- 7 The molecule of claim 6 wherein the nucleotide sequences encoding the cystic fibrosis trans-membrane conductance regulator comprise exon 10 of the cystic fibrosis trans-membrane regulator conductance gene.
- 8. A recombinant expression vector wherein said vector expresses a nucleotide sequence comprising:
 - a) two or more target binding domains that target binding of the pretrans-splicing molecule to a target pre-mRNA;
 - a 3' splice region comprising a branchpoint, a pyrimidine tract and
 a 3' splice acceptor site and a 5' splice donor site;
 - c) spacer regions that separate the 3' splice region and the 5' splice donor site from the target binding domains; and
 - d) a nucleotide sequence to be trans-spliced to the target pre-mRNA; wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.
- 9. The molecule of claim 1 or 8 further comprising a safety nucleotide sequence comprising one or more complementary sequences that bind to one or more sides of the pre-trans-splicing molecule branch point, pyrimidine tract, 3' splice site or 5' splice site.
- 10. A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:
 - a) two or more target binding domains that target binding of the pretrans-splicing molecule to a target pre-mRNA:
 - b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site and a 5' splice donor site;
 - c) spacer regions that separate the 3' splice region and the 5' splice donor site from the target binding domains; and



- 11. The cell of claim 10 wherein the spacer regions of the nucleic acid molecule separate the 3' splice region and the 5' splice donor site from the target binding domains.
- 12. The cell of claim 10 wherein the nucleic acid molecule further comprises sequences encoding a translatable protein product.
 - 13. The cell of claim 12 wherein translatable protein is a toxin.
- 14. The cell of claim 10 wherein the nucleic acid molecule further comprises a nucleotide sequence containing a translational stop codon.
- 15. The cell of claim 10 wherein the nucleotide sequence to be *trans*-spliced to the target pre-mRNA comprises nucleotide sequences encoding the cystic fibrosis transmembrane conductance regulator.
- 16. The cell of claim 10 wherein the nucleotide sequences encoding the cystic fibrosis transmembrane conductance regulator comprise exon 10 cystic fibrosis transmembrane conductance regulator gene.
- 17. A cell comprising a recombinant expression vector wherein said vector expresses a nucleotide sequence comprising:
 - a) two or more target binding domains that target binding of the pretrans-splicing molecule to a target pre-mRNA;
 - b) a 3' splice region comprising a branchpoint, a pyrimidine tract and

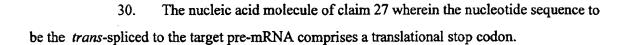
- a 3' splice acceptor site and a 5' splice donor site;
- c) spacer regions that separate the 3' splice region and the 5' splice donor site from the target binding domains; and
- a nucleotide sequence to be trans-spliced to the target pre-mRNA;
 wherein said nucleic acid molecules is recognized by nuclear
 splicing components within the cell.
- 18. A cell comprising the nucleic acid molecule of claim 1 or 8 further comprising a safety nucleotide sequence comprising one or more complementary sequences that bind to one or more sides of the pre-trans-splicing molecule branch point, pyrimidine tract, 3' splice site or 5' splice site.
- 19. A method of producing a chimeric mRNA molecule comprising contacting a pre-trans-splicing molecule with a target pre-mRNA under conditions in which a double *trans*-splicing reaction results in a portion of the pre-*trans*-splicing molecule being *trans*-spliced to a portion of the target pre-mRNA to form said chimeric mRNA.
- 20. The method of claim 19 wherein the pre-trans-splicing mRNA comprises nucleotide sequences encoding the cystic fibrosis transmembrane conductance regulator.
- 21. The method of claim 19 wherein the pre-trans-splicing mRNA comprises exon 10 cystic fibrosis transmembrane conductance regulator gene.
- 22. A method of providing a host cell with a chimeric mRNA molecule, said method comprising:

transferring a pre-trans-splicing molecule to a host cell expressing a target pre-mRNA wherein the pre-trans-splicing molecule binds to the target pre-mRNA under conditions in which a double trans-splicing reaction results in a portion of the pre-trans-splicing molecule being trans-spliced to a portion of the target pre-mRNA to form said chimeric mRNA.

- 23. The method of claim 20 wherein the host cell is a human cell.
- 24. The method of claim 20 wherein the pre-trans-splicing molecule comprises nucleotide sequences encoding a protein that is defective or lacking in the host cell.
- 25. The method of claim 22 wherein the pre-trans-splicing molecule comprises nucleotide sequences encoding a fragment of the cystic fibrosis trans-membrane regulator protein.
- 26. A pharmaceutical composition comprising the nucleic acid molecule of claim 1 and a pharmaceutically acceptable carrier.
 - 27. A nucleic acid molecule comprising:
 - a) one or more target binding domains that target binding of the pretrans-splicing molecule to a target pre-mRNA;
 - b) a 5' splice donor site;
 - a spacer region that separates the 5' splice donor site from the target binding domain; and
 - a nucleotide sequence comprising the 5' end of a gene to be transspliced to the target pre-mRNA;

wherein said nucleic acid molecules is recognized by nuclear splicing components within the cell.

- 28. The nucleic acid molecule of claim 27 wherein the nucleotide sequence to be the *trans*-spliced to the target pre-mRNA encodes a translatable protein product.
- 29. The nucleic acid molecule of claim 28 wherein the translatable protein product is a toxin.



- 31. The nucleic acid molecule of claim 27 wherein the nucleotide sequence to be *trans*-spliced to the target pre-mRNA comprises nucleotide sequences encoding the cystic fibrosis transmembrane conductance regulator.
- 32. The nucleic acid molecule of claim 27 wherein the nucleotide sequences encoding the cystic fibrosis transmembrane conductance regulator comprise exons 1-10 cystic fibrosis transmembrane regulator gene.
- 33. A recombinant expression vector wherein said vector expresses a nucleotide sequence comprising:
 - a) one or more target binding domains that target binding of the pretrans-splicing molecule to a target pre-mRNA;
 - b) a 5' splice donor site;
 - a spacer region that separates the 5' splice donor site from the target binding domain; and
 - a nucleotide sequence comprising the 5' end of a gene to be transspliced to the target pre-mRNA;

wherein said nucleic acid molecules is recognized by nuclear splicing components within the cell.

- 34. The molecule of claim 27 or 30 further comprising a safety nucleotide sequence comprising one or more complementary sequences that bind to one or more sides of the pre-trans-splicing molecule branch point, pyrimidine tract, or 3' splice site.
- 35. The recombinant expression vector of claim 33 further comprising a safety nucleotide sequence comprising one or more complementary sequences that bind to one or more

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sides of the pre-trans-splicing molecule branch point, pyrimidine tract, or 3' splice site.

- 36. A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:
 - a) one or more target binding domains that target binding of the pretrans-splicing molecule to a target pre-mRNA;
 - b) a 5' splice donor site;
 - c) a spacer region that separates the 5' splice donor site from the target binding domain; and
 - a nucleotide sequence comprising the 5' end of a gene to be transspliced to the target pre-mRNA;

wherein said nucleic acid molecules is recognized by nuclear splicing components within the cell.

- 37. The cell of claim 32 wherein the nucleic acid molecule further comprises sequences encoding a translatable protein product.
- 38. The cell of claim 36 wherein the nucleic acid molecule further comprises a nucleotide sequence containing a translational stop codon.
- 39. The cell of claim 36 wherein the nucleotide sequence to be *trans*-spliced to the target pre-mRNA comprises nucleotide sequences encoding the cystic fibrosis transmembrane regulator.
- 40. The cell of claim 39 wherein the nucleotide sequences encoding the cystic fibrosis trans-membrane regulator comprise exons 1-10 of the cystic fibrosis transmembrane regulator gene.
 - 41. The cell of claim 37 wherein the translatable protein is a toxin.



- 42. A cell comprising a recombinant expression vector wherein said vector expresses a nucleotide sequence comprising:
 - a) one or more target binding domains that target binding of the pretrans-splicing molecule to a target pre-mRNA;
 - b) a 5' splice donor site;
 - c) a spacer region that separates the 5' splice donor site from the target binding domain; and
 - a nucleotide sequence comprising the 5' end of a gene to be transspliced to the target pre-mRNA;

wherein said nucleic acid molecules is recognized by nuclear splicing components within the cell.

- 43. A cell comprising the nucleic acid molecule of claim 27 or 37 further comprising a safety nucleotide sequence comprising one or more complementary sequences that bind to one or more sides of the pre-trans-splicing molecule branchpoint, pyrimidine tract, or 5' splice site.
- 44. A cell comprising the recombinant expression vector of claim 33 further comprising a safety nucleotide sequence comprising one or more complementary sequences that bind to one or more sides of the pre-trans-splicing molecule branchpoint, pyrimidine tract, or 5' splice site.
- 45. A method of producing a chimeric mRNA molecule comprising contacting a pre-trans-splicing molecule with a target pre-mRNA under conditions in which a trans-splicing reaction results in a portion of the pre-trans-splicing molecule being trans-spliced to the 5' end of the target pre-mRNA to form said chimeric mRNA.
 - 46. The method of claim 45 wherein the pre-trans-splicing mRNA comprises

nucleotide sequences encoding the cystic fibrosis transmembrane conductance regulator.

- 47. The method of claim 46 wherein the pre-trans-splicing mRNA comprises exons 1-10 of the cystic fibrosis transmembrane conductance regulator gene.
- 48. A method of providing a host cell with a chimeric mRNA molecule, said method comprising:

transferring a pre-trans-splicing molecule to a host cell expressing a target pre-mRNA wherein the pre-trans-splicing molecule binds to the target pre-mRNA under conditions in which a trans-splicing reaction results in a portion of the pre-trans-splicing molecule being trans-spliced to a 5' portion of the target pre-mRNA to form said chimeric mRNA.

- 49. The method of claim 48 wherein the host cell is a human cell.
- 50. The method of claim 48 wherein the pre-trans-splicing molecule comprises nucleotide sequences encoding a protein that is defective or lacking in the host cell.
- 51. The method of claim 50 wherein the pre-trans-splicing molecule comprises nucleotide sequences encoding a fragment of the cystic fibrosis transmembrane conductance regulator protein.
- 52. A pharmaceutical composition comprising the nucleic acid molecule of claim 27 and a pharmaceutically acceptable carrier.
 - 53. A nucleic acid molecule wherein said nucleic acid molecule is CFTR PTM24.